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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/585,772	11/13/2007	Aiping H. Young	50120/008001	4680

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EXAMINER	
SHIN, DANA H	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
04/02/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

Office Action Summary	Application No.	Applicant(s)	
	10/585,772	YOUNG ET AL.	
	Examiner	Art Unit	
	DANA SHIN	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34 and 52-55* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 52-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7-12-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of claims 18-34 pertaining to SEQ ID NO:1 ("Group 103") in the reply filed on March 4, 2009 is acknowledged. The traversal is on the ground(s) that the prior art reference of Lee et al. does not teach "the use of immunotherapeutic agents" for the claimed SEQ ID NO:1. This is not found persuasive because the term "immunotherapeutic agent" recited in claim 1 means immunologic therapy that enhances the immune system's responses to cancer cells during cancer therapy. See page 2 of the instant application. The reference of Lee et al. expressly taught that the antisense of SEQ ID NO:1 is not only an anti-tumor agent useful for cancer therapy but also a potential immune stimulator, thereby contributing to the "overall antitumor efficacy" of SEQ ID NO:1. See page 2807, right column. Hence, the teachings of Lee et al. clearly suggest a combination of an antisense of SEQ ID NO:1 and an immunotherapeutic agent because the enhanced, overall antitumor efficacy of SEQ ID NO:1 was also contributed by immunotherapeutic properties of the SEQ ID NO:1. Hence, it is concluded that the claimed invention does not contribute a special technical feature when viewed over the prior art of Lee et al., and thus lacks unity of invention. Applicant's attention is directed to the fact that the generic claims (see for example, claim 20 drawn to SEQ ID NO:105) will be fully examined as well, and therefore the examination of claims 18-20 and 23-34 is not limited to SEQ ID NO:1.

The requirement is still deemed proper and is therefore made FINAL.

Status of Claims

Claims 1-34 and 52-55 are currently pending in the instant application. Claims 1-17 and 52-55 as well as SEQ ID NOs:4-104 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Accordingly, claims 18-34 pertaining to SEQ ID NO:1 are currently under examination on the merits in the instant case.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/535,496, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. It is found that the disclosure of 60/535,496 fails to provide adequate support for the instantly claimed step of administering "(b) one or more immunotherapeutic agents" in addition to administering an antisense oligonucleotide. The disclosure of 60/602,817 filed on August 18, 2004 appears to be the first earlier-filed application

that provides adequate support for the claimed invention. Accordingly, the benefit of an earlier filing date for claims 18-34 is granted only insofar as the filing date of 60/602,817.

If applicant believes the disclosure of 60/535,496 provides adequate support for claims 18-34 in the manner provided by the first paragraph of 35 U.S.C. 112, applicant is advised to point out the particulars in response to this Office action.

Claim Objections

Claim 21 is objected to for containing non-elected subject matter. Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-20, 23, 25, 28-29, and 33-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Wright et al. (WO 98/00532, applicant's citation).

The claims are drawn to a combination therapeutic method for treating a metastatic cancer in a mammal comprising administering an antisense oligonucleotide of 7-100 nucleotides in length complementary to a mammalian ribonucleotide reductase R2 subunit mRNA of SEQ ID NO:105 and one or more specific immunotherapeutic agents that are monoclonal antibodies, wherein the antisense oligonucleotide comprises phosphorothioates.

Wright et al. teach a method of treating a metastatic cancer or a solid cancer in a mammal comprising administering a pharmaceutical composition comprising 1) a phosphorothioate-modified antisense oligonucleotide that is at least 7 consecutive nucleotides complementary to SEQ ID NO:43, which is 39 nucleotides in length and is complementary to nucleotides 2007-2045 of SEQ ID NO:105 of the instant application and 2) specific antibodies such as monoclonal antibodies, wherein the mammal is a human. See pages 7, 11, 13-16; claims 7, 8, 10-13, 26-30. Accordingly, all claim limitations are taught by Wright et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 18-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (*Cancer Research,* 2003, 63:2802-2811, citation of record, also applicant's citation) in view of Hatanaka et al. (*The Journal of Gene Medicine,* 2004, 6:1139-1148).

The claims are drawn to a method of treating cancer in a human comprising administering (a) a phosphorothioate-containing antisense oligonucleotide of SEQ ID NO:1 and (b) one or more cytokines as a first-line systemic therapy, further comprising administering one or more chemotherapeutic agents, wherein the cancer is a solid cancer, advanced cancer, and metastatic cancer.

Lee et al. teach that a phosphorothioate-modified antisense oligonucleotide of "GTI-2040" whose nucleotide sequence is identical to SEQ ID NO:1 of the instant application is a potential therapeutic agent for cancer treatment as they show that "GTI-2040" reduces tumor growth and metastasis in mammals. They suggest that the antitumor efficacy of "GTI-2040" may in part, but not significantly, be contributed by immune stimulatory effect of "GTI-2040". They teach that "GTI-2040" has finished a Phase I clinical trial with favorable results and that a combination therapy with standard chemotherapeutic drugs is another potential therapeutic strategy for a broad range of cancers. They further describe that chemotherapy or cytokine therapy alone has limited efficacy. See pages 2802-2803, 2806-2810. Lee et al. do not teach a combination therapy comprising "GTI-2040" and a cytokine as a first-line systemic therapy.

Hatanaka et al. teach a combination therapy for treating metastatic or advanced pancreatic cancer in a mammal by administering an antisense oligonucleotide together with a cytokine, IFN-α. They show that the antisense and IFN-α combination therapeutic strategy results in a significant synergistic pancreatic cancer cell growth inhibition in a mammal. They

suggest that the antisense and IFN-α combination can be used as a systemic therapy for metastasis-prone, systemic cancers. They also describe that cancer treatment comprising a cytokine in combination with standard chemotherapeutic drugs have shown to be potential cancer treatment strategy by recent clinical trials. See pages 1140-1147.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the antisense anti-cancer agent of "GTI-2040" of Lee et al. in the method of combination cancer therapy of Hatanaka et al.

One of ordinary skill in the art would have been motivated to treat cancer in a cancer patient by administering "GTI-2040" of Lee et al. together with a cytokine IFN-α so as to achieve a synergistic anti-cancer therapeutic effect for treating advanced, metastatic cancer because Hatanaka et al. taught that antisense and IFN-α combination therapy results in a significant synergistic cancer growth inhibition effect in a mammal, and because the antisense agent of "GTI-2040" of Lee et al. was an art-recognized anti-cancer therapeutic agent tested in human patients. Furthermore, one of ordinary skill in the art would have been motivated to enhance the anti-cancer efficacy of "GTI-2040" by virtue of increasing immune stimulation, one of inherent properties of "GTI-2040", by adding an immune stimulatory agent, for example, IFN-α, because Lee et al. taught that the overall anti-cancer effect of "GTI-2040" was partially achieved by its inherent immune stimulatory property. Taken together, the instantly claimed cancer treatment method comprising "GTI-2040" (identical to the claimed antisense of SEQ ID NO:1 in the instant case) and a cytokine IFN-α would have naturally flowed from the teachings of Lee et al. and Hatanaka et al. In addition, one of ordinary skill in the art attempting to further increase anti-tumor activity or treat a broad range of cancers would have been motivated to add

one or more chemotherapeutic agents to the "GTI-2040"-IFNα combination therapy because Lee et al. expressly suggested that combining "GTI-2040" with chemotherapeutic agents is a potential treatment method for treating a broad range of cancers since chemotherapy or cytokine therapy alone has limited efficacy, and because Hatanaka et al. taught that combination cancer therapy methods comprising a cytokine and standard chemotherapeutic drugs were actively tested for enhanced anti-tumor activity during clinical trials. As such, since combining chemotherapeutic agents with either "GTI-2040" or a cytokine for cancer therapy was one of the sought-after treatment options by the researchers in the art, one of ordinary skill in the art would have reasonably added standard chemotherapeutic drugs to the combination of "GTI-2040"-IFNα. Since both knowledge and skills to arrive at the claimed combination treatment method were within the technical grasp of one of ordinary skill in the art at the time the invention was made, one of ordinary skill in the art would have had a reasonable expectation of success in treating advanced, metastatic, or solid cancer in a cancer patient by administering "GTI-2040" and IFNα, further administering standard chemotherapeutic drugs to the cancer patient. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Claims 18-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et al. (US 5,998,383) in view of Pavlick et al. (*Expert opinion on Investigational Drugs,* 2003, 12:1546-1558).

The claims are described above.

Wright et al. teach a combination cancer treatment method in a mammal comprising administering a chemotherapeutic drug and an antisense oligonucleotide of SEQ ID NO:42, which is identical in sequence to SEQ ID NO:1 of the instant application, wherein the cancer treatment method inhibits cell growth and metastasis of tumor cells in a human patient. They teach that the combination treatment method can be used to treat various forms of cancer including a metastatic cancer and a solid cancer. They teach that the antisense oligonucleotide comprises phosphorothioate linkages for increased nuclease resistance. See columns 6-12; Table 7; claims 11-13, 18-20, 30-31. Wright et al. do not teach a combination therapy further comprising immunotherapeutic agents.

Pavlick et al. teach various cancer therapeutic strategies that have been explored and clinically tested in the art, especially for treating malignant, advanced, metastatic cancer. They describe that conventional treatments such as chemotherapy and radiation are not sufficient to treat such malignant, advanced, metastatic cancer, and therefore a number of different combination therapeutic strategies have been devised. They teach that one of the first combination therapies explored in the art is concurrent "biochemotherapy" clinical trials comprising immunotherapy (e.g., administering non-specific cancer vaccines, specific cancer vaccines, cytokine-adjuvants, antibodies, or cytokines) combined with conventional chemotherapy (e.g., administering cisplatin, vinblastine, or dacarbazine). They teach that combination therapeutic strategies further comprising a target-specific antisense oligonucleotide agent are also promising because of the low toxicity and low side-effect profiles of the antisense oligonucleotide agent. See the entire reference including Table 3.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to devise a first-line systemic combination cancer therapeutic strategy of administering

the antisense anti-cancer agent of SEQ ID NO:42 of Wright et al. and immunotherapeutic agents, further comprising chemotherapeutic agents.

One of ordinary skill in the art would have been motivated to do so in order to increase the therapeutic efficacy of a single anti-cancer agent-based therapy (e.g., antisense alone, chemotherapy alone, immunotherapy alone) for treating advanced, malignant, and metastatic cancer, because the problem and inadequacy of singe anti-cancer agent-based therapy for treating such advanced, malignant, and metastatic cancer were recognized in the art and a new cancer treatment design was thus needed in the art, and because only a finite number of identified, predictable potential solutions (e.g., antisense agent combined with chemotherapy, immunotherapy combined with chemotherapy, antisense agent combined with any cancer therapeutic strategies) were recognized in the art as taught by Wright et al. and Pavlick et al. Since the clinical efficacy and safety of the antisense agent of Wright et al. (identical to the instantly claimed antisense agent of SEQ ID NO:1) were known in the art for cancer treatment, and since one of ordinary skill in the art would have had good reason to pursue one of the known options for combination cancer treatment methods for enhanced therapeutic outcome, wherein one of the options is the combination comprising immunotherapy and antisense agent as first-line systemic therapy, further comprising chemotherapy, and since such combination cancer therapeutic strategy was within the technical grasp of the ordinary skilled artisan at the time of the invention, as evidenced by the state of the art and technology described by Wright et al., and Pavlick et al., one of ordinary skill in the art would have had a reasonable expectation of success in arriving at the claimed invention. Accordingly, the claimed invention taken as a whole would have been *prima facie* obvious at the time of filing.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DANA SHIN whose telephone number is (571)272-8008. The examiner can normally be reached on Monday through Friday, 7am-3:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Dana Shin
Examiner
Art Unit 1635

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